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POSTGRADUATE MEDICAL SCHOOL
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Telegrams
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Telephone
SHEpherds Bush 1260 (4 lines)

DUCANE ROAD
LONDON, W.12

Department of
Bacteriology.

8th April, 1952.

Dear Dr. Lederberg,

I had intended to write you a detailed letter when I had some leisure after the Soc. Gen. Microbiol. meeting next week but have been prompted to do so now by a letter from Cavalli this morning saying that you and he would like to publish your paper on F+ transduction in the J. Gen. Microbiol., preferably in the same issue as mine would appear, and that your joint paper should be ready by the end of the month. Let me say at once that I think this is very nice of you both and that I will be only too pleased to co-operate. However, I don't want to appear in any way Machiavellian (which I am not!) and thought I should let you know at once of some recent work which I have done which I <u>think</u> seriously undermines any orthodox interpretation of recombination in K-12 as a more or less classical sexual process. I am afraid I cannot go into experimental detail now but can only give you a resume of my results. However I feel that my technique and method are sound and that you can accept the results as valid. Incidentally, let me say in advance that my "unorthodoxy" is largely due to a poor knowledge of classical genetics so that I do not instinctively interpret findings in genetic terms. I do not hold strongly to my theory and am quite ready to abandon it if need be, and I cannot attempt to fit my findings into a <u>detailed</u> genetic picture without expert advice.

/According to you

1. According to you, F+ is separate from the "gamete" and determines self-compatibility; i.e. determines the ability of the two mutants to mate by means of a more or less orthodox sexual mechanism in which both partners participate more or less equally. If this is so, then F+ x F+ matings should be more efficient that F+ x F- matings since, in the former, all the cells are compatible ab initio, while in the latter, mating must occur in two stages - first the transduction of F+ to the F- cells and then the actual mating between the now compatible F+ cells. On putting this to the test, I found that 58-161/F+ x W677/F+ is approximately twenty times less efficient in prototroph formation than either 58-161/F+ x W677/F- or W677/F+ x 58-161/F-. I have repeated this twice and am confident that it is so.

2. As I see it, if recombination is achieved by the union of two complete haploid chromosomes, with crossing over and meiosis, then the patterns of unselected markers should be the same irrespective of which partner of the mating mixture initially carries F+ or F-. I have in the past tested several hundred prototroph colonies from the usual 58-161/F+ x W677/F- mate and have been struck by the fact that 25 - 30 per cent have the W677 ("gene acceptor") phenotype. The markers I have used have been Lac, Man, ØT1 and ØT3. I have now tested 20 prototroph

/Colonies from each

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just a useful word!

colonies from each of the F+ x F+ and F+ x F- matings specified above. I find that, using these markers, the majority of prototrophs carry the phenotype of the F- ("gene acceptor") strain and none that of the F+ strain when one of the strains is frankly F- while in the F+ x F+ cross the phenotype of the prototrophs is (apart from "new" strains) either that of 58-161 or of W677 in about equal proportions. These results are quite clearcut and, although I have only done this experiment once, I am sure that they will prove repeatable.

I shall be most interested to learn your views. At the moment I am trying to formulate my own for my forthcoming paper. I still hold that an F+ strain is one which harbours a "gamete" and, like lysogenic cells in relation to phage, cannot receive one until it has got rid of its own; while F- cells are "gamete"-free. I think it possible that some of the "blocks" of genes which the "gamete" carries can perhaps show genuine recombination with parts of the F- chromosome but that the basic genetic structure of the prototroph remains that of the "acceptor" strain. Perhaps the number of "" are an index of the vagueness of my views but I feel that the details are really a matter for the geneticist. It may be that the K-12 type of recombination is the missing link in the evolution of sexual mechanisms from simple transformations and all the more interesting on that account.

Spicer tells me that he is going to work in your lab. in the near future. I would very much like to have the opportunity to discuss things with you personally but can't see a hope of getting to America in the forseeable future. But perhaps you will be coming to Europe! I thought your "Selected Papers" excellent and a most valuable book to possess.

Yours sincerely,